Remarks/Arguments

The foregoing amendments to the claims are of formal nature, and do not add new matter. Prior to the present amendment, claims 39-51 were pending in this application and were rejected on various grounds. Claims 1-38 were previously canceled in a preliminary amendment and claim 48 was previously canceled without prejudice. Claims 39-44 have been amended, support for which can be found in Example 77, page 210, lines 22 onwards. In addition, claims 45-47 and 49 have been amended to correct minor typographical errors. Entry of these amendments are respectfully requested. The rejection to the presently pending claims are respectfully traversed.

Priority

Applicants rely on the skin vascular permeability assay (Example 77) to establish patentable utility for polypeptide PRO326. These results were first disclosed in international application PCT/US98/19437, filed 17 September, 1998 to which priority is claimed in this application. Support for this is found on page 52, line 26 of the PCT/US98/19437 application. Accordingly, the present application is entitled to the effective filing date of 17 September, 1998.

Formal Matters

The title was objected to as "not descriptive." The new title added by the foregoing amendment is believed to overcome this objection.

Claims 45-49 were objected to for lacking a period (.) following the claim numbers. The claims have been amended accordingly.

Applicants thank the Examiner for acknowledging the compliance of the biological organism deposit according to the terms of the Budapest Treaty and for considering the information disclosure statement.

Double Patenting

Claims 39-44, 46-48 and 50-51 were provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over the claims of copending Application No. 09/903520 (drawn to PRO335).

As Applicants have already filed a terminal disclaimer in the related copending Application No. 09/903520, this rejection is moot.

Thus, Applicants respectfully request that this obviousness-type double patenting rejection be withdrawn.

Claim Rejections – 35 USC §101

Claims 39-51 were rejected under 35 U.S.C. §101 allegedly because the claimed invention was not supported by either a specific, substantial and credible asserted utility or a well established utility.

Utility - Legal Standard

According to the Utility Examination Guidelines ("Utility Guidelines"), 66 Fed. Reg. 1092 (2001) an invention complies with the utility requirement of 35 U.S.C. § 101, if it has at least one asserted "specific, substantial, and credible utility" or a "well-established utility." Under the Utility Guidelines, a utility is "specific" when it is particular to the subject matter claimed. For example, it is generally not enough to state that a nucleic acid is useful as a diagnostic without also identifying the conditions that is to be diagnosed.

The requirement of "substantial utility" defines a "real world" use, and derives from the Supreme Court's holding in *Brenner v. Manson*, 383 U.S. 519, 534 (1966) stating that "The basic *quid pro quo* contemplated by the Constitution and the Congress for granting a patent monopoly is the benefit derived by the public from an invention with substantial utility." In. explaining the "substantial utility" standard, M.P.E.P. 2107.01 cautions, however, that Office personnel must be careful not to interpret the phrase "immediate benefit to the public" or similar formulations used in certain court decisions to mean that products or services based on the claimed invention must be "currently available" to the public in order to satisfy the utility requirement. "Rather, **any reasonable use that an applicant has identified for the invention that can be viewed as providing a public benefit should be accepted as sufficient**, at least with regard to defining a "substantial" utility." (M.P.E.P. 2107.01, emphasis added.) Indeed, the Guidelines for Examination of Applications for Compliance With the Utility Requirement, set forth in M.P.E.P, 2107 II (B) (1) gives the following instruction to patent examiners: "If the applicant has asserted that the claimed invention is useful for any particular practical purpose ... and the assertion would

be considered credible by a person of ordinary skill in the art, do not impose a rejection based on lack of utility."

Finally, the Utility Guidelines restate the Patent Office's long established position that any asserted utility has to be "credible." "Credibility is assessed from the perspective of one of ordinary skill in the art in view of the disclosure and any other evidence of record ... that is probative of the applicant's assertions." (M.P.E.P. 2107 II (B) (1) (ii)) Such standard is presumptively satisfied unless the logic underlying the assertion is seriously flawed, or if the facts upon which the assertion is based are inconsistent with the logic underlying the assertion (Revised Interim Utility Guidelines Training Materials, 1999).

Proper Application of the Legal Standard

As discussed above, Applicants rely on the skin vascular permeability assay (Assay 64 or Example 77, page 210, lines 22 onwards) for priority and to establish patentable utility for polypeptide PRO326. These results were first disclosed in international application PCT/US98/19437, filed 17 September, 1998 to which priority is claimed in this application. Accordingly, the present application is entitled to the effective filing date of 17 September, 1998.

The claims as presently amended recite polypeptides that induce an immune or inflammatory response.

Example 77 (assay 64) describes a dye-based proinflammatory cell infiltration assay in skin in which PRO326 induces mononuclear cell, eosinophil and PMN infiltration into the site of injection of this peptide/protein into an animal. Here, purified or conditioned media containing PRO326 was injected intradermally onto the backs of hairless guinea pigs whereas the Evans blue dye was injected intracardially. Blemishes at the injection sites were measured 1 h and 6 h post injection. Animals were sacrificed at 6 h after injection, the skin at each injection site was biopsied, fixed in formalin and evaluated histopathologically for inflammatory cell infiltration into the skin. Such inflammatory cell infiltration assays are routinely used in the art to evaluate proinflammatory properties of novel compounds (see Rampart et al; enclosed in IDS). For example, in Rampart et al. (see Methods, page 22), IL-8 (Interleukin 8) was identified using a similar neutrophil accumulation assay in rabbit skin and the findings were correlated with albumin flux and neutrophil dependent edema in skin.

Under proinflammatory conditions, several mechanisms act synergistically to mediate an increase in neutrophil accumulation, plasma extravasation, etc. Such events occur for example, during the acute phase of an inflammatory response to a microbial stimulus or during pathologic conditions like graft rejection, edema, psoriasis, arthritis, tissue injury etc. The enclosed reference, Rampart et al. suggests the involvement of endogenous IL-8 in an acute phase inflammatory response of an animal to a microbial stimulus and further disclosed suggestive data supporting its involvement in psoriasis (see page 24, column 1, last paragraph). Subsequent data affirmed the involvement of IL-8 in several inflammatory conditions and in immune response; for example: IL-8 has been shown to be part of the cytokine cascade in the synovium of patients suffering from rheumatoid arthritis, IL-8 is also associated with other inflammatory diseases like asthma, leprosy, psoriasis, inflammatory bowel disease, atherosclerosis, cystic fibrosis, and in various respiratory syndromes. Similarly, a variety of real-life utilities are envisioned for PRO326 based on the proinflammatory cell infiltration assay results disclosed herein. Thus, contrary to the Examiner's assertion, the skin vascular permeability assay is not merely a hypersensitive assay. Instead, results from this assay have been used to identify molecules useful in treating inflammatory diseases and immune diseases.

As set forth in M.P.E.P, 2107 II (B) (1), if the applicant has asserted that the claimed invention is useful for any particular practical purpose, and the assertion would be considered credible by a person of ordinary skill in the art, a rejection based on lack of utility should not be imposed. Indeed, the logic underlying Applicants' assertion that PRO326 may be useful in boosting an immune response is not inconsistent with the general knowledge in the art, and would be considered credible by a person skilled in the art. It is always possible that an invention might fail on its way of development to a commercial product. For example, despite recent advances in rational drug design, a large percentage of drug candidates fails, and never makes it into a drug product. However, the USPTO is not the FDA, the law does not require that a drug product be currently available to the public in order to satisfy the utility requirement.

Accordingly, the Examiner is respectfully requested to reconsider and withdraw the present rejection.

Claim Rejections – 35 USC § 112- Enablement and Written Description

Claims 39-51 were rejected under 35 U.S.C. §112, first paragraph, since allegedly, the specification was not supported by either a specific, substantial and credible asserted utility and one skilled in the art would not know hoe to use the claimed invention. Applicants respectfully traverse this rejection.

Claims 39-43 and 52-51 were rejected under 35 U.S.C. §112, first paragraph, as allegedly containing subject matter not described in the specification in such a way as to convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. Applicants respectfully traverse.

Present claim amendments recite polypeptides that induce an immune or inflammatory response. Support for this recitation is found in Example 77 (page 210, lines 22) which describes a dye-based proinflammatory cell infiltration assay in which PRO326 induces mononuclear cell, eosinophil and PMN infiltration into the site of injection of this peptide/protein into an animal. The Examiner has acknowledged that the results of Example 77 provide the skilled artisan with guidance on how to use such a polypeptide (Office Action, page 6, line 12-14).

In view of the present claim amendments, the claims are now drawn to a genus of polypeptides defined both by sequence and functional identity. Based on the information disclosed in the specification and that which was available in the art, one skilled in the art knew how to practice the claimed invention, at the effective priority date of this application, without undue experimentation. As the M.P.E.P. states, "The fact that experimentation may be complex does not necessarily make it undue, if the art typically engages in such experimentation. *In re Certain Limited-charge cell Culture Microcarriers, 221 USPQ 1165, 1174* (Int'l Trade Comm'n 1983), *aff'. sub nom., Massachusetts Institute of Technology v A.B. Fortia,* 774 F.2d 1104, 227 USPQ 428 (Fed. Cir. 1985) M.P.E.P. 2164.01. One of skill in the art also knew that the Applicants had possession of the claimed molecules at the time of filing.

Hence, the Examiner is respectfully requested to reconsider and withdraw the present rejection.

Prior Art

Since the effective filing date for the instant application is 17 September, 1998, U.S.P.N. 6,426,072 (dated 8/21/00), Locii Q9D332 (dated 6/1/01) and O94898 (dated 5/1/99) are not available as prior art.

Also, the instant claims are not anticipated by a protein having 50% identity to SEQ ID NO: 5 from USPN 6,046,030 (dated 12/8/97) nor by Locus P70193 (dated 2/1/97) since the instant claims recite and claim proteins with 80%, 85%, 90%, 95%, 99% identity and additionally, since claimed polypeptides recite a functional recitation of inducing an immune or inflammatory response, neither of which is not taught in the prior art.

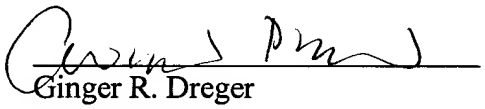
Hence, neither of the cited prior art anticipate the presently claimed subject matter.

The present application is believed to be in *prima facie* condition for allowance, and an early action to that effect is respectfully solicited.

Please charge any additional fees, including any fees for additional extension of time, or credit overpayment to Deposit Account No. 08-1641 (Attorney Docket No.: 39780-1618P2C27). Please direct any calls in connection with this application to the undersigned at the number provided below.

Respectfully submitted,

Date: August 29, 2003



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Paper No.

Notice of Non-Compliant Amendment (Voluntary Revised Practice)

The amendment filed 7-23-03 under the voluntary revised amendment practice guidelines[1], published in the Official Gazette on February 25, 2003 (*Amendments in a Revised Format Now Permitted,* 1267 Off. Gazette 106), does not fully comply with minimal requirements of the voluntary practice. In order for the amendment to be entered, it must either (1) comply with the guidelines of the voluntary revised amendment practice (which practice invokes waivers of certain 37 CFR 1.121(a)-(d) requirements) or (2) comply with current 37 CFR 1.121 requirements.

THE FOLLOWING ITEM(S) IN APPLICANT'S AMENDMENT CAUSES THE AMENDMENT TO BE NON-COMPLIANT WITH THE VOLUNTARY REVISED AMENDMENT PRACTICE.

☑ 1. A complete listing of all of the claims is not present in the amendment paper.

☐ 2. The listing of claims does not include the text of all claims currently under examination.

☐ 3. The claims of this amendment paper have not been presented in ascending numerical order.

☑ 4. Each claim has not been provided with a status identifier, and, as such, the individual status of each claim cannot be determined.

☑ 5. Other: Shows no markup-version of claims

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LIE: Check one of the following boxes:

☐ **PRELIMINARY AMENDMENT:** Applicant is given ONE MONTH from the mail date of this letter to re-submit the amendment in compliance with either the guidelines of the revised amendment practice or current 37 CFR 1.121. Failure to comply with either the current 37 CFR 1.121 practice or with the voluntary practice will result in non-entry of the amendment and examination on the merits will commence without entry of the originally proposed preliminary amendment. This notice is not an action under 35 U.S.C. 132, and this ONE MONTH time limit is not extendable.

☑ **AMENDMENT AFTER NON-FINAL ACTION:** Since the above-mentioned reply appears to be a *bona fide* response, applicant is given a TIME PERIOD of ONE MONTH from the mailing of this notice within which to re-submit an amendment which complies with either the voluntary practice guidelines or current 37 CFR 1.121 in order to avoid abandonment. EXTENSIONS OF THIS TIME PERIOD ARE AVAILABLE UNDER 37 CFR 1.136(a).

[Signed by Team Leader]
Team Leader

[1] For further explanation of the guidelines of the revised amendment format, please see the posted notice and sample amendment format at: http://www.uspto.gov/web/offices/pac/dapp/opla/preognotice/officeflyer.pdf and http://www.uspto.gov/web/offices/pac/dapp/opla/preognotice/formatrevamdtprac.pdf